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Introduction dynamical system modelling

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Modelling infectious disease epidemics, analysis and response

Short course. Bogota. 11-15th December 2017

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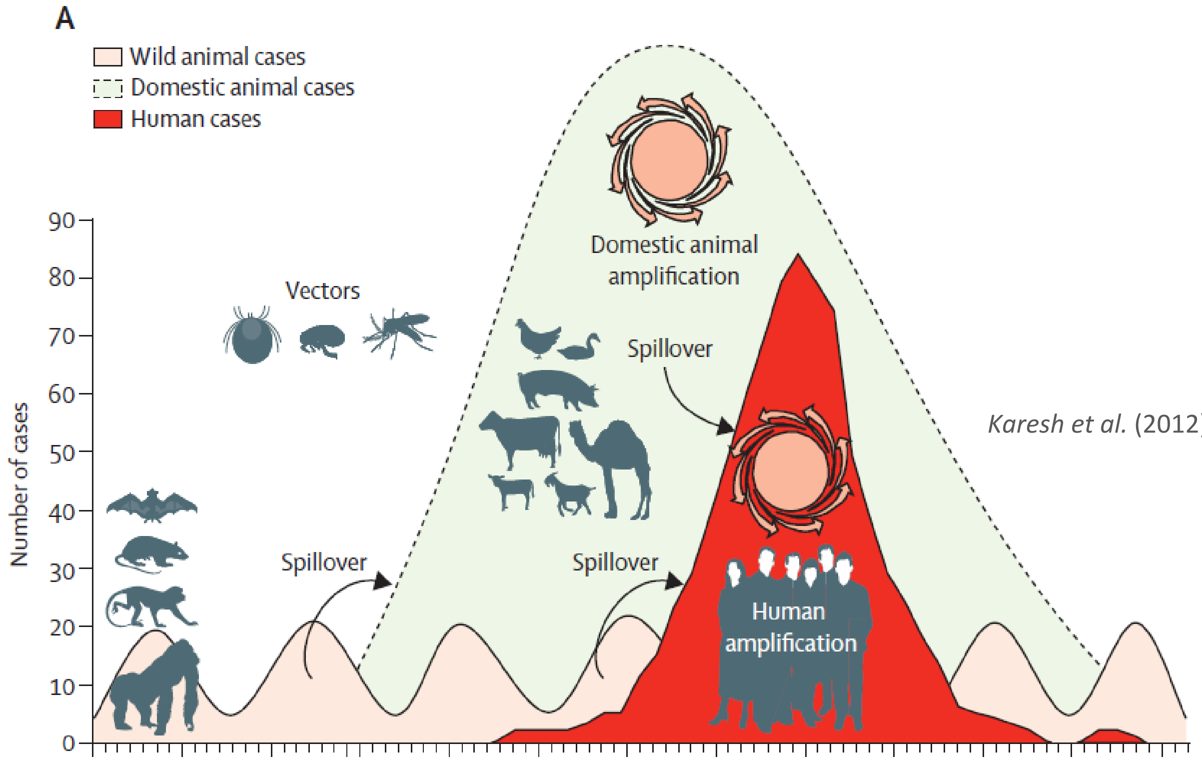
Understanding the dynamics of ID

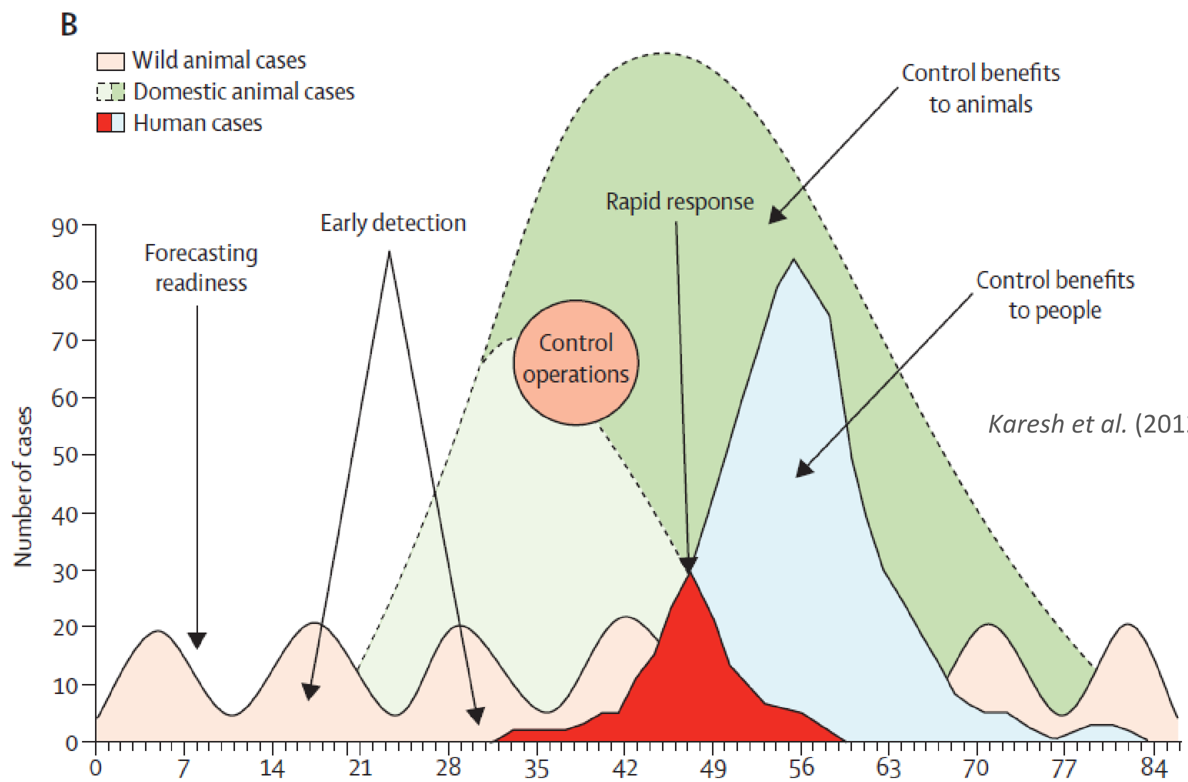
Being prepared and responding promptly require understanding the dynamics of the disease



Karesh et al. (2012) Lancet

Understanding the dynamics of ID

Being prepared and responding promptly require understanding the dynamics of the disease



Karesh et al. (2012) Lancet

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Objectives

- Introduction to concepts in quantitative epidemiology of infectious diseases

- Understand the dynamics of epidemics
- Understanding key parameters
- Modelling control

- Application to Ebola

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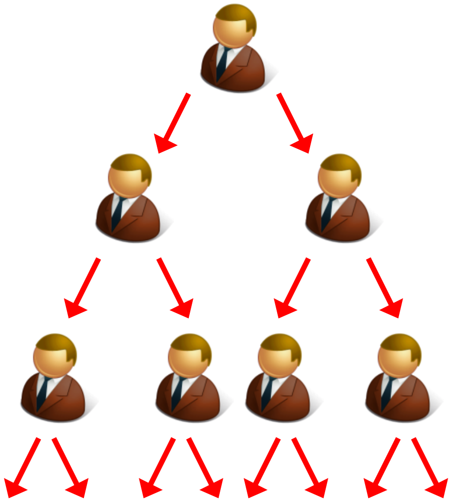
Objectives, details

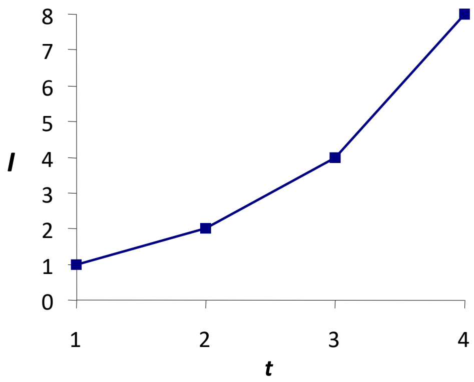
- Exponential growth
- Epidemic curve
- Flow diagrams – dynamical system
- Contact rate
- Model SEI
- Reproduction number
- Models for Ebola

Exponential growth

- One dog is infected.
- He will infect other.
- Who will infect more.
- We obtain a chain reaction:

  an epidemic



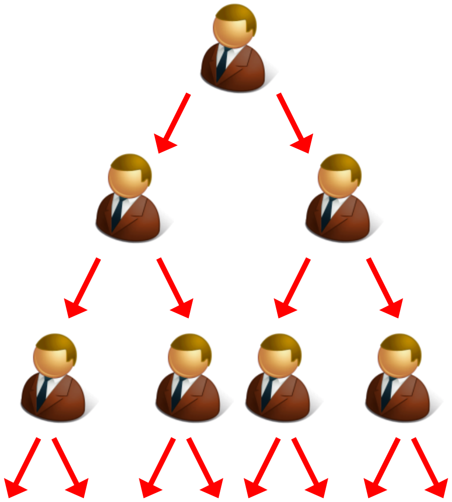


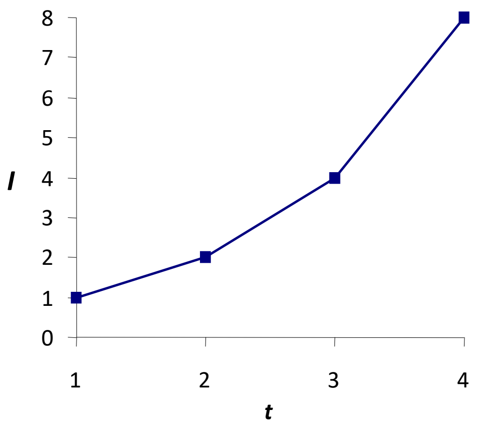
Exponential growth

$t=0, \quad I_0 = 1$

$t=1, \quad I_1 = 2$

$t=2, \quad I_2 = 4$



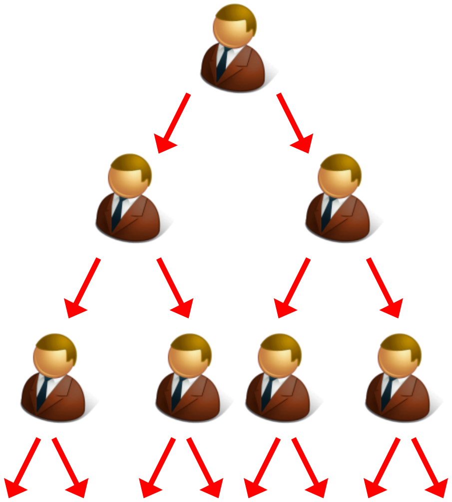


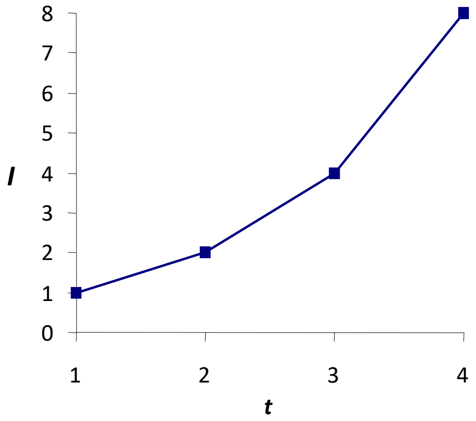
Exponential growth

$t=0, \quad I_0 = 1$

$t=1, \quad I_1 = 2 = I_0 \times 2$

$t=2, \quad I_2 = 4 = I_1 \times 2$





Exponential growth

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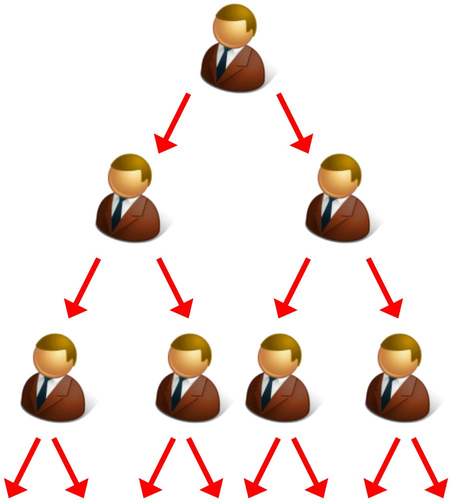

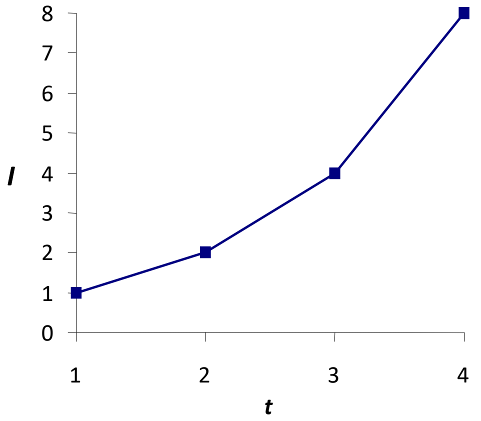

Exponential growth: $I_t = I_0 \times 2^t = I_0 \times e^{r\,t}$

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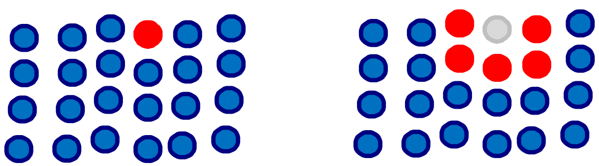
Epidemic curve

Healthy   Infected   Dead or recovered



t=0   t=1

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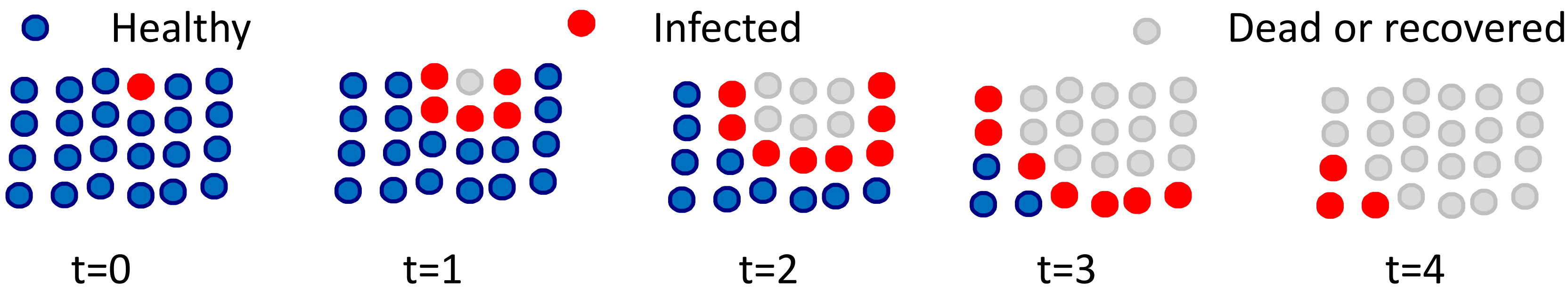
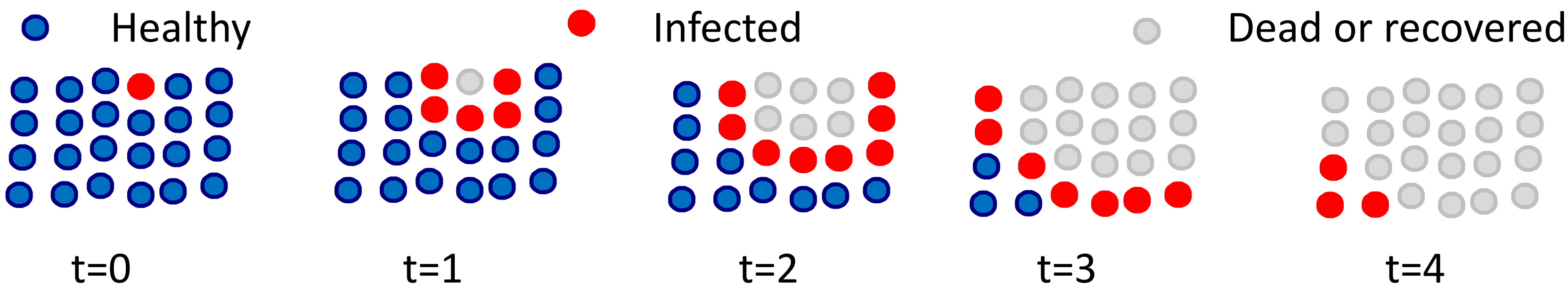
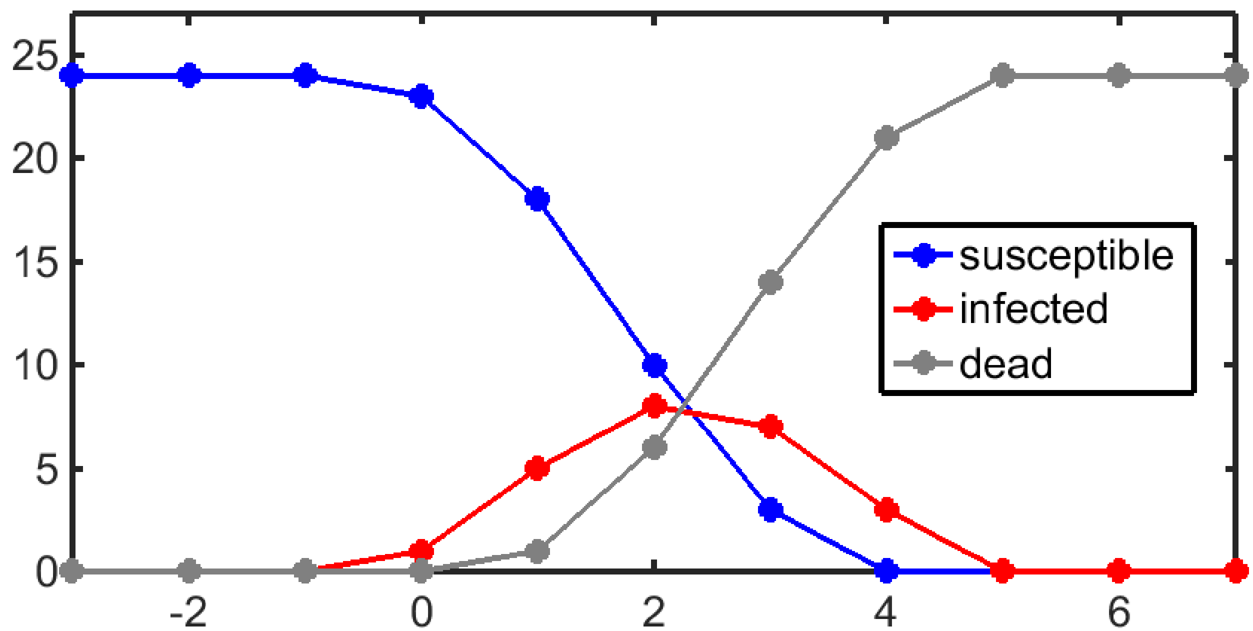
Epidemic curve

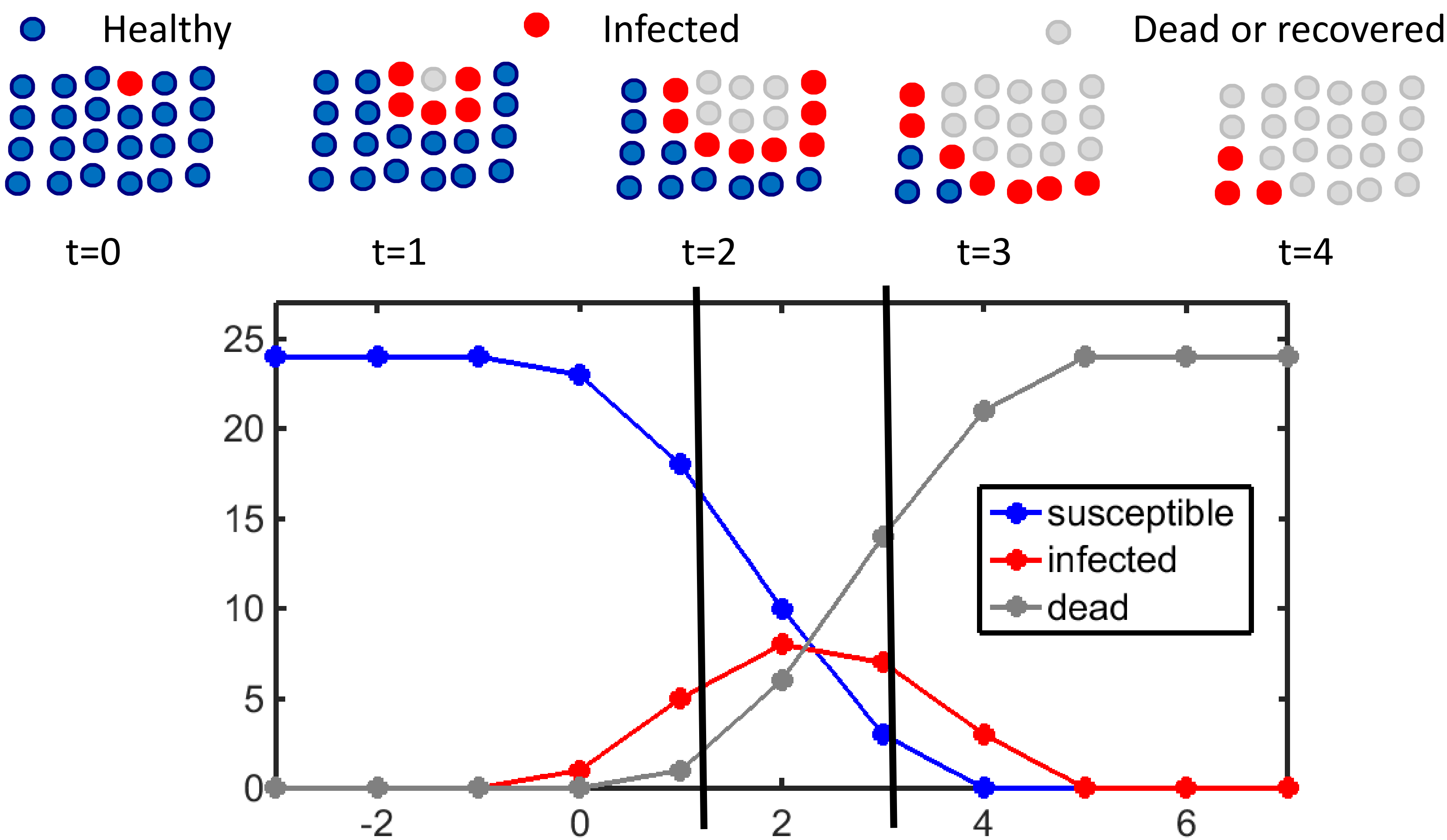


Epidemic curve

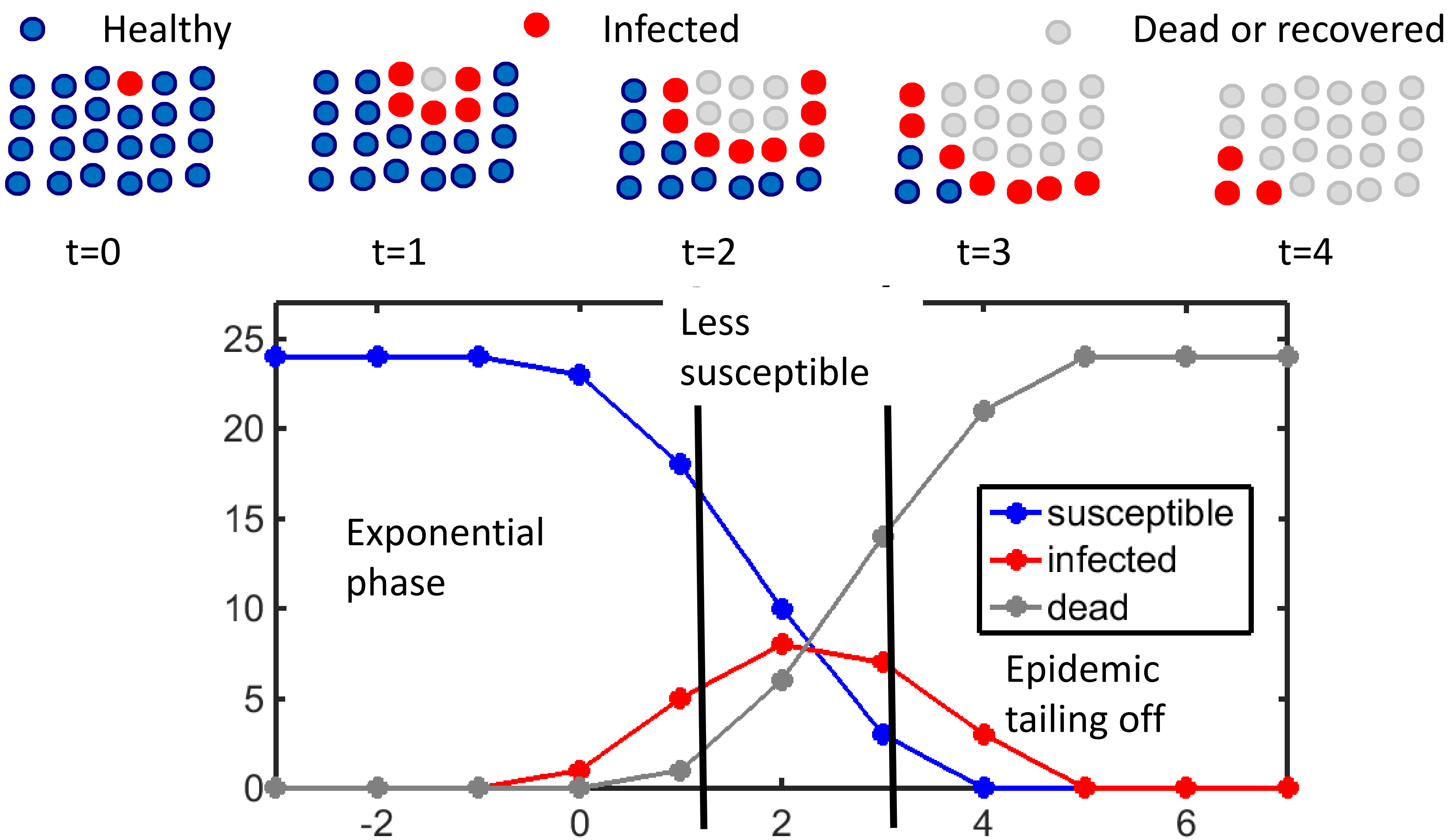




Epidemic curve



Epidemic curve



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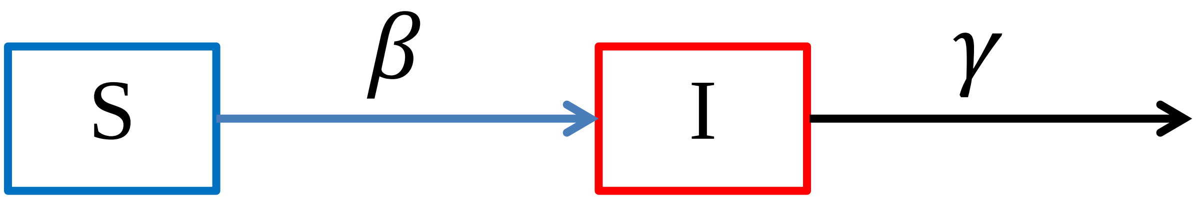
Flow diagram

Healthy   Infected   Dead or recovered



Model SI:

$$S_t = S_{t-1} - \frac{\beta}{N} S_{t-1} I_{t-1}$$

$$I_t = I_{t-1} + \frac{\beta}{N} S_{t-1} I_{t-1} - \gamma I_{t-1}$$

β : transmission rate

$\frac{\beta}{N} S_{t-1} I_{t-1}$: new infections

γ: recovery or death rate

γI_{t-1}: nb of recoveries/deaths

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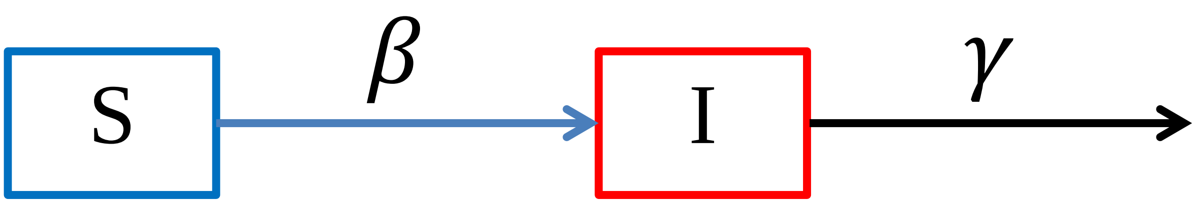
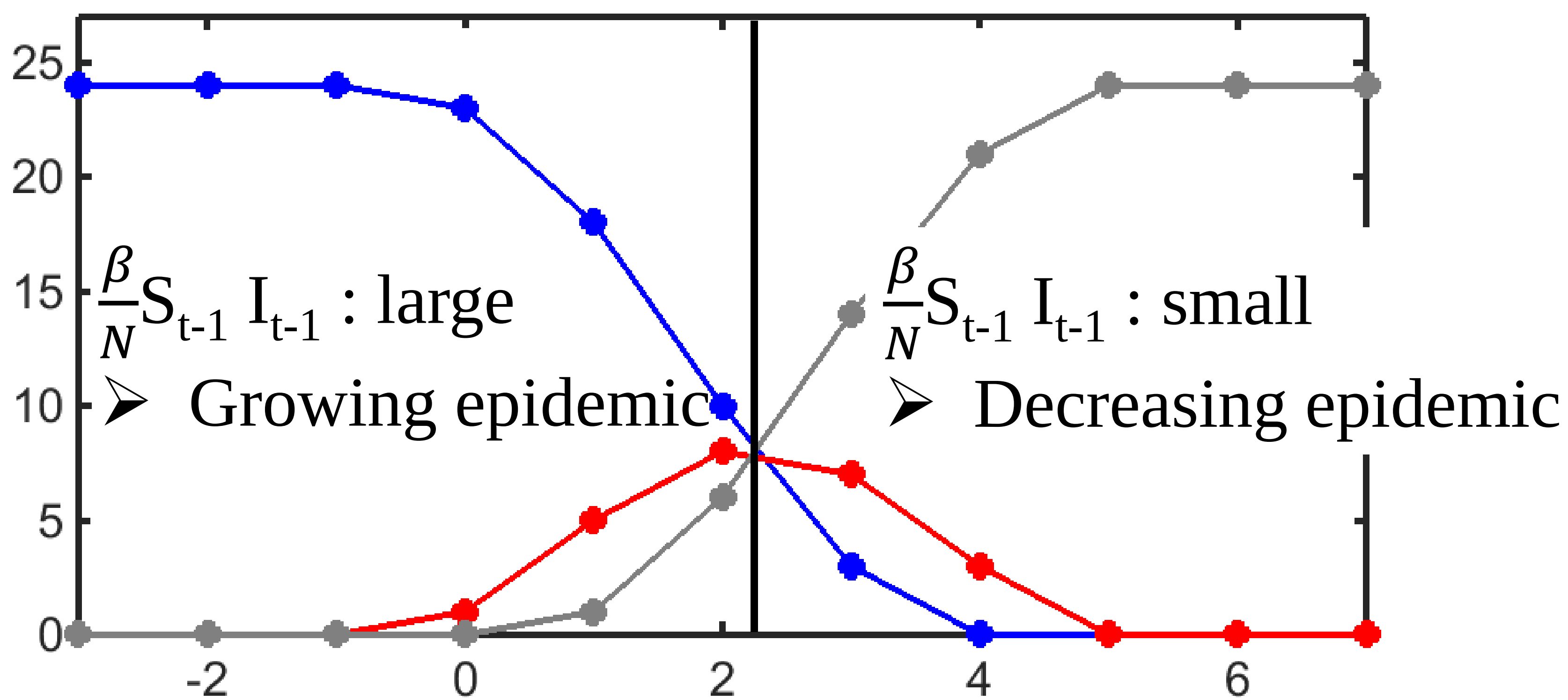
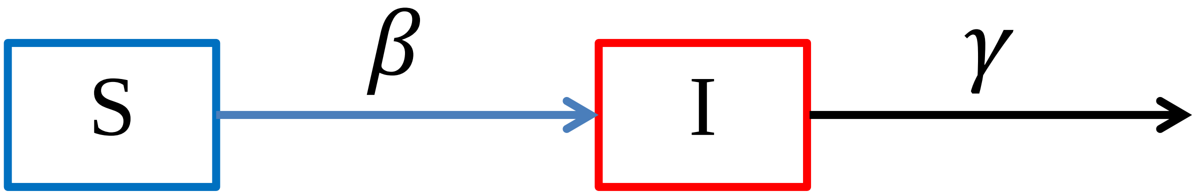
Flow diagram





Flow diagram



Model SI, discrete time

$$S_t = S_{t-1} - \frac{\beta}{N} S_{t-1} I_{t-1}$$

$$I_t = I_{t-1} + \frac{\beta}{N} S_{t-1} I_{t-1} - \gamma I_{t-1}$$

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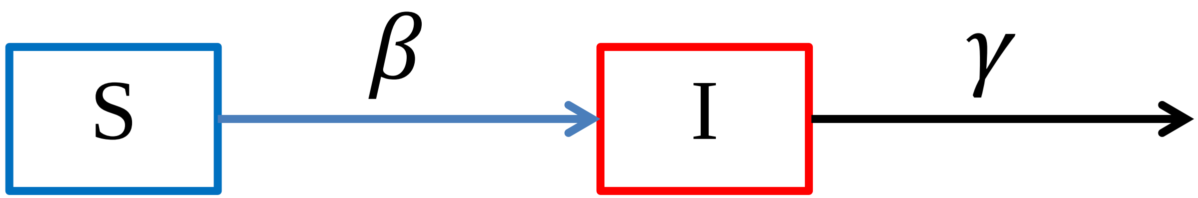
Flow diagram



Model SI, discrete time

$$S_t = S_{t-1} - \frac{\beta}{N} S_{t-1}\, I_{t-1}$$

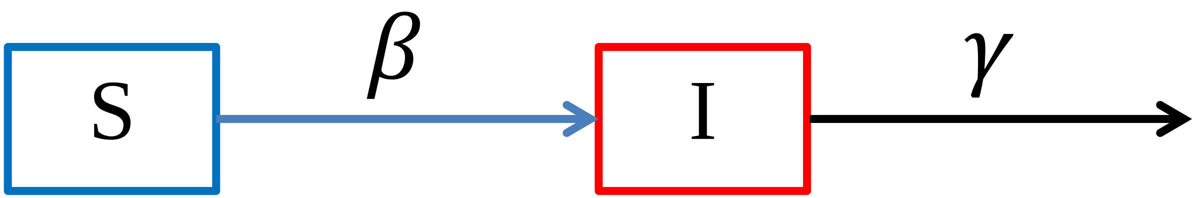
$$I_t = I_{t-1} + \frac{\beta}{N} S_{t-1}\, I_{t-1} - \gamma I_{t-1}$$

Continuous time

$$\frac{dS}{dt} = -\frac{\beta}{N} S_t I_t$$

$$\frac{dI}{dt} = \frac{\beta}{N} S_t I_t - \gamma I_t$$

Flow diagram



During dt

dS: change in susceptibles

dI: change in infectious

Continuous time

$$\frac{dS}{dt} = -\frac{\beta}{N} S_t I_t$$

$$\frac{dI}{dt} = \frac{\beta}{N} S_t I_t - \gamma I_t$$

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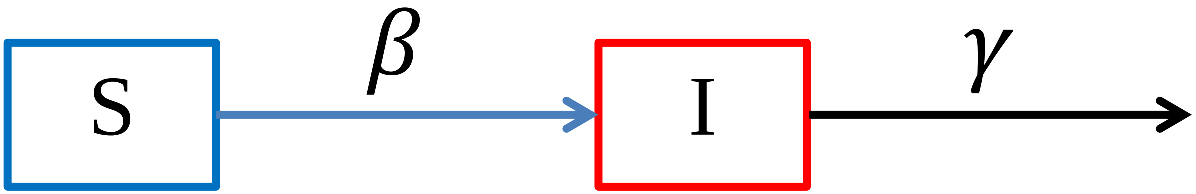

Model SI

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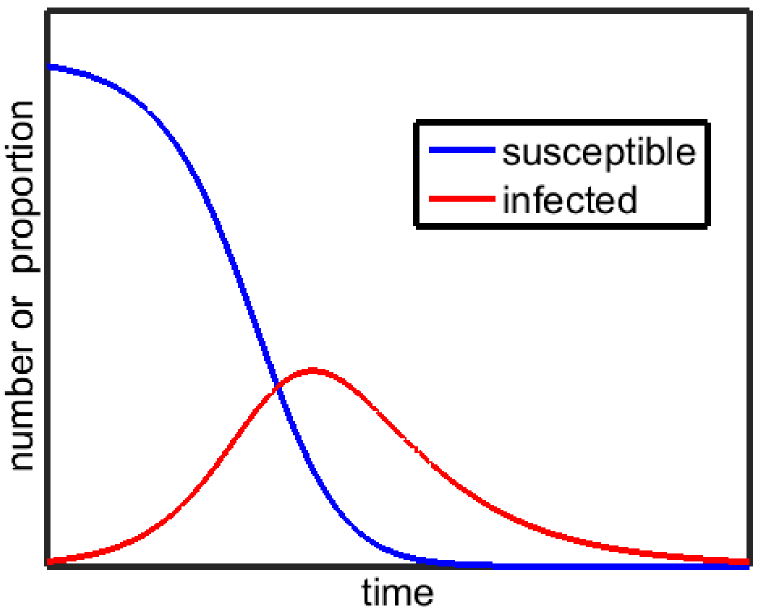

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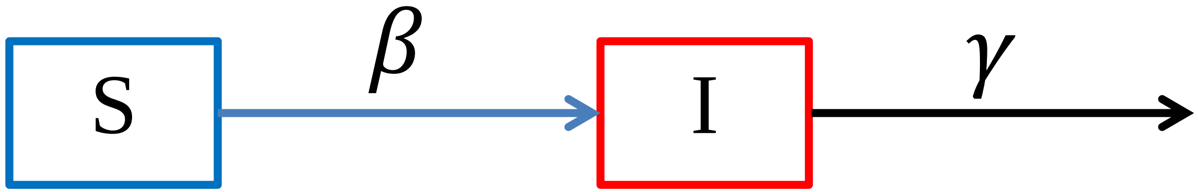
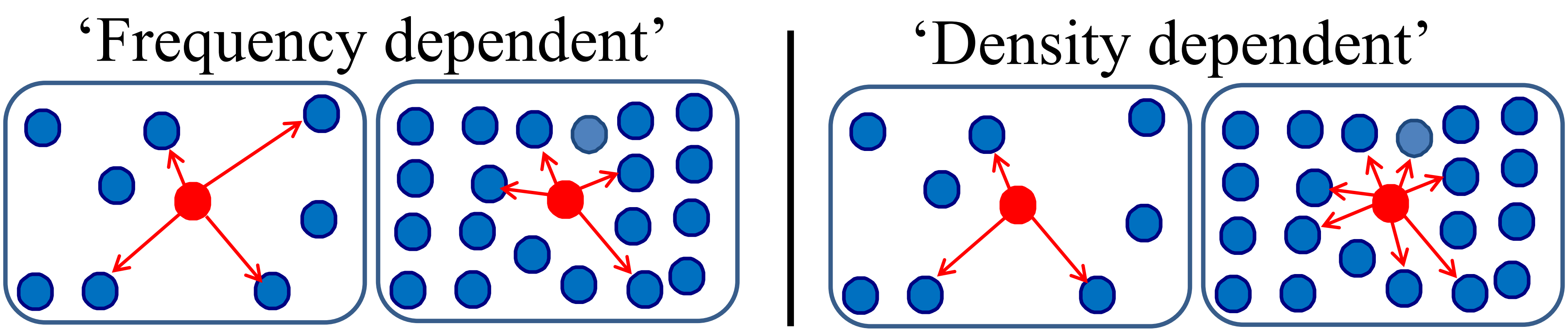
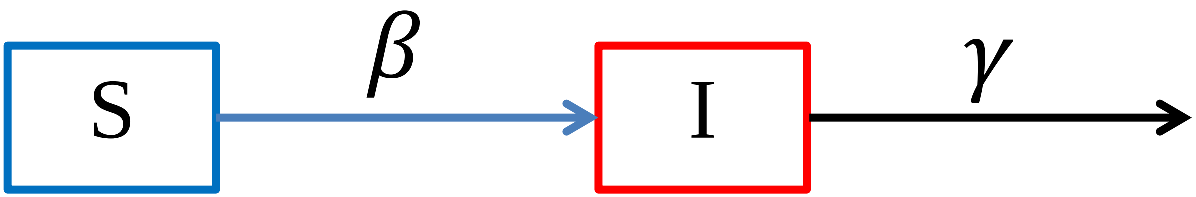
Characterise contacts



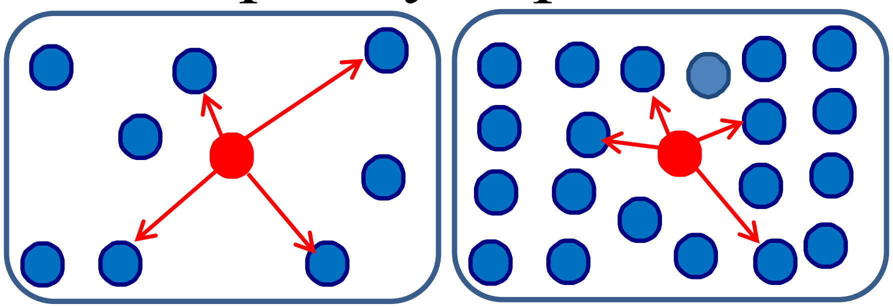
1. The number of contact is fixed, regardless of density
    - ➢ Frequency dependent contacts
2. The number of contact increase with density
    - ➢ Density dependent contact



Characterise contacts



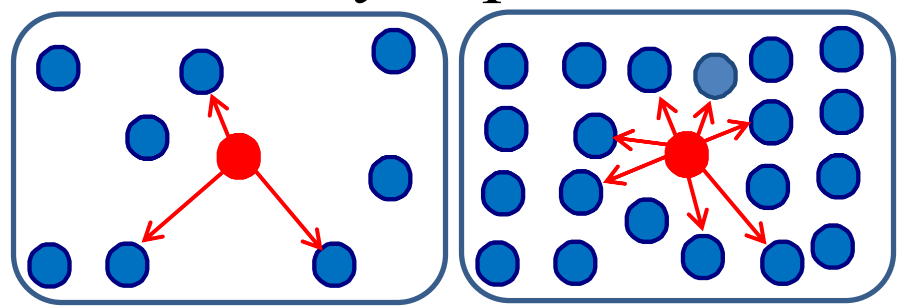
‘Frequency dependent’



Model

$$\frac{dS}{dt} = -\frac{\beta}{N} S_t I_t$$

‘Density dependent’



Model

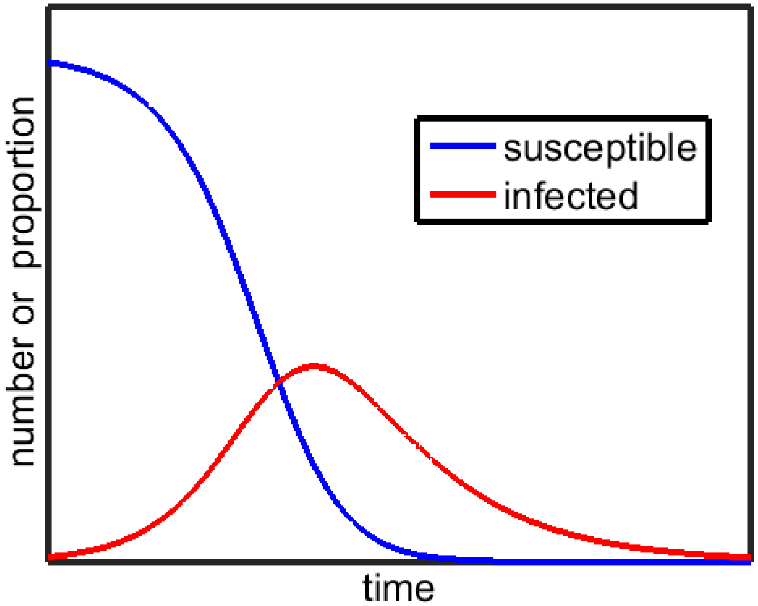
$$\frac{dS}{dt} = -\beta \, S_t I_t$$

Characterise contacts

Implications for the epidemic curve

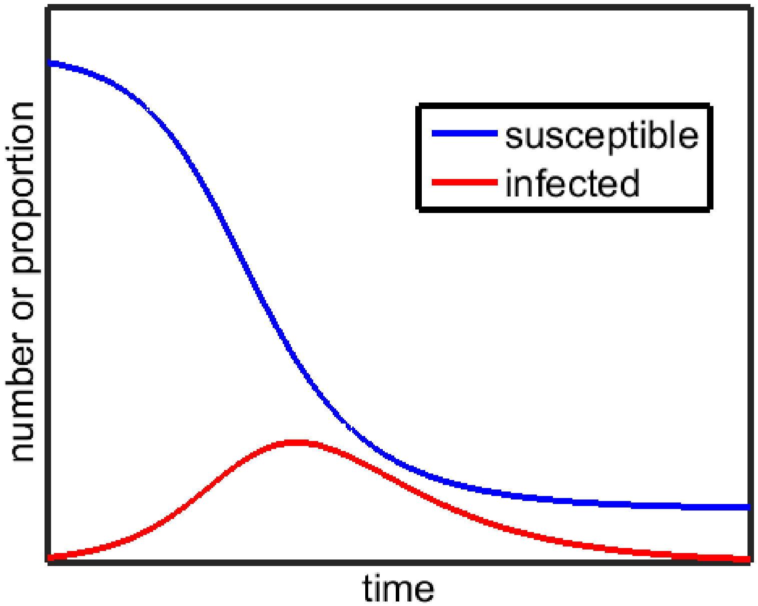
‘Frequency dependent’

$$\frac{dS}{dt} = -\frac{\beta}{N} S_t I_t$$



‘Density dependent’

$$\frac{dS}{dt} = -\beta\, S_t I_t$$



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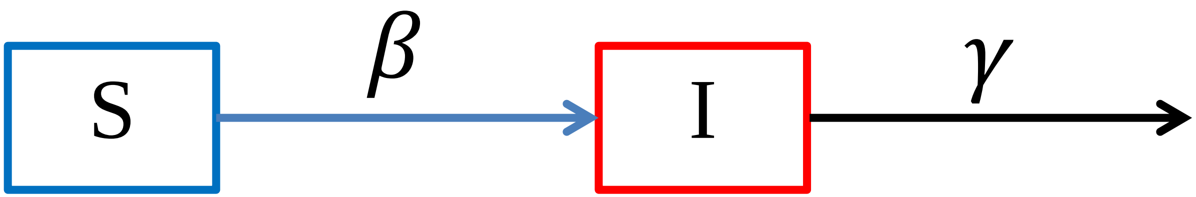
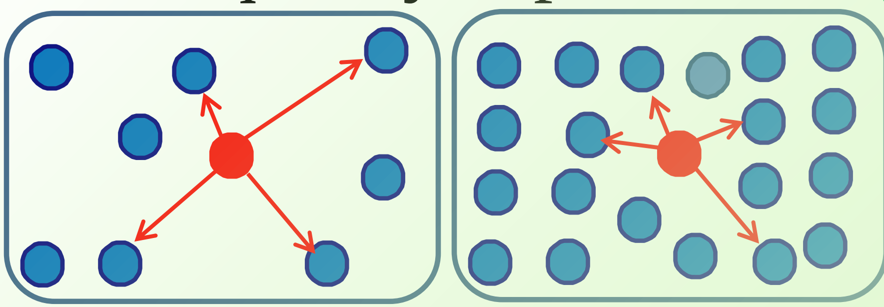
Characterise contacts



'Frequency dependent'

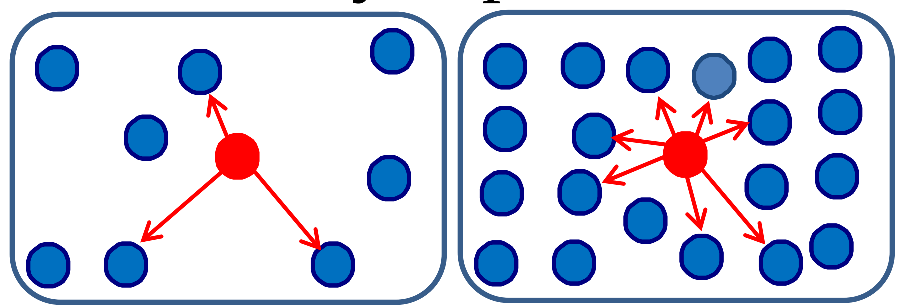


Ebola

Model

$$\frac{dS}{dt} = -\frac{\beta}{N} S_t I_t$$

'Density dependent'



Model

$$\frac{dS}{dt} = -\beta\, S_t I_t$$

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Reproduction number

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Definition:

Average number of secondary cases generated by an index case in a ***large entirely susceptible*** population

$$R_0 = \beta D = pcD$$

- β: Transmission rate
- p: Transmission probability
- c: Contact rate
- D: Duration of infectiousness

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Reproduction number

Contact rate

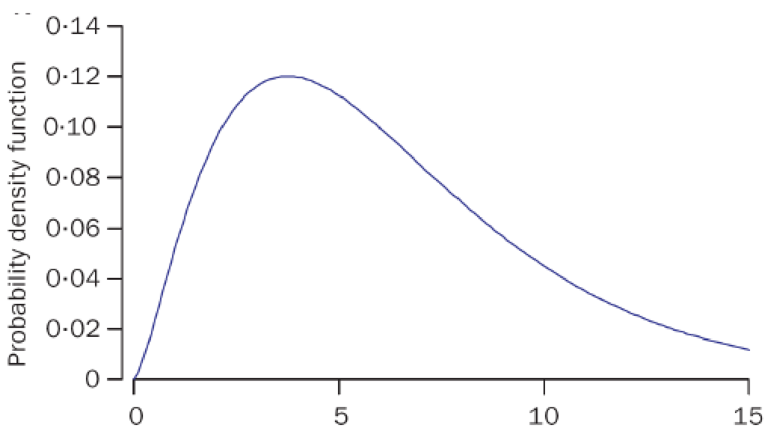
Transmission rate

Transmission probability

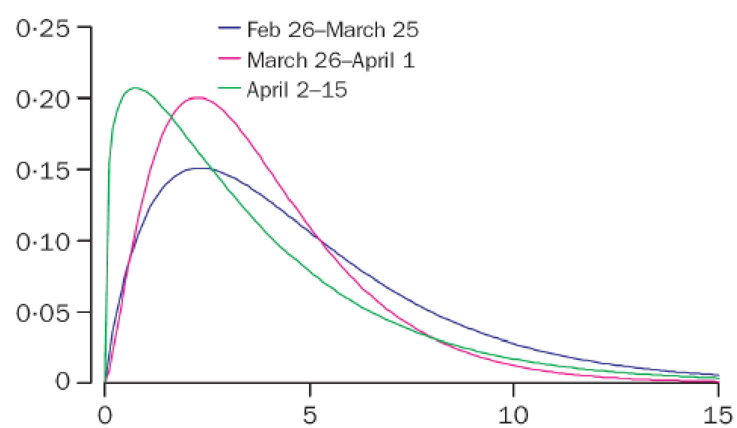
$$R_0 = \beta D = pcD$$

Duration of infectiousness

Duration of infectiousness: context dependent



Time from onset to recovery (or death)



Time from onset to isolation (SARS)

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Reproduction number

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Contact rate

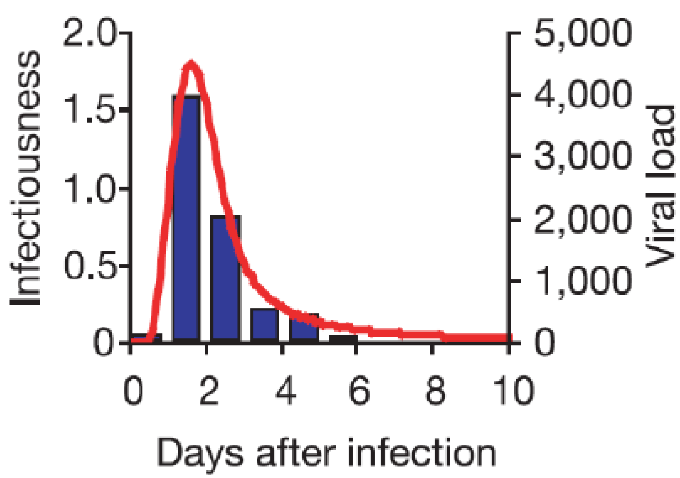
Transmission rate

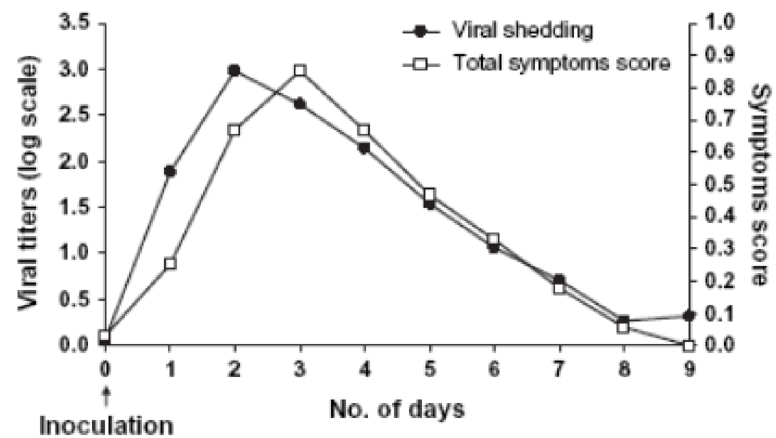
Transmission probability

$$R_0 = \beta D = pcD$$

Duration of infectiousness

Transmission rate: very difficult to estimate





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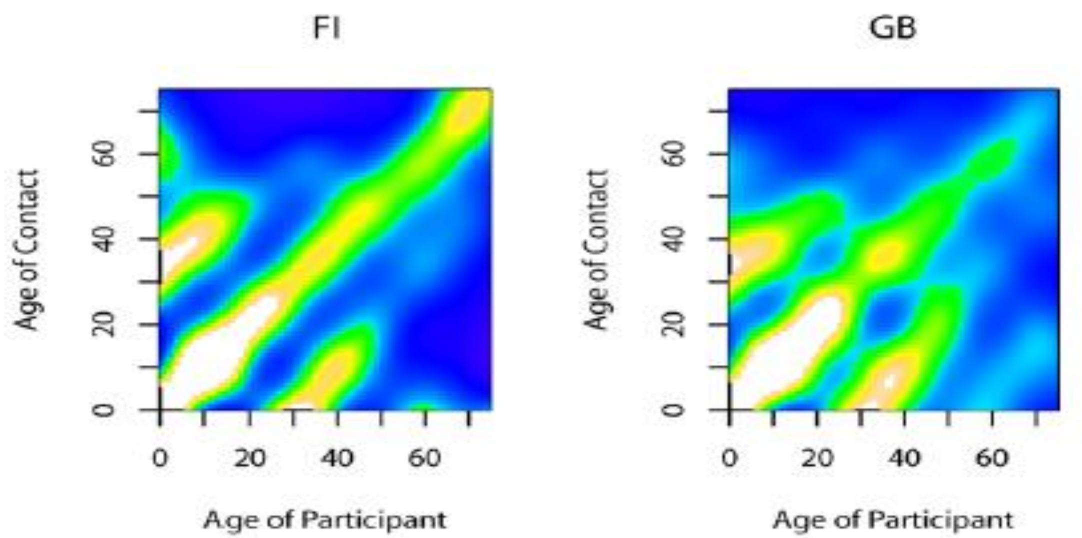
Reproduction number

$$R_0 = \beta D = pcD$$

- Transmission rate: β
- Transmission probability: p
- Contact rate: c
- Duration of infectiousness: D

Contact rate: needs clear definition of infectious contact



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Reproduction number

Contact rate

Transmission rate

Transmission probability

$$R_0 = \beta D = p c D$$

Duration of infectiousness

Deriving R0 from compartmental models

Reproduction number

Deriving R0 from compartmental models

Model SI

$$\frac{dS}{dt} = -\frac{\beta}{N} S_t I_t$$

$$\frac{dI}{dt} = \frac{\beta}{N} S_t I_t - \gamma I_t$$

Overall transmission rate:

$$\frac{\beta}{N} S_t I_t$$

Duration of infectiousness:

$$\frac{1}{\gamma}$$

Reproduction number

Deriving R0 from compartmental models

Model SI

$$\frac{dS}{dt} = -\frac{\beta}{N} S_t I_t$$

$$\frac{dI}{dt} = \frac{\beta}{N} S_t I_t - \gamma I_t$$

With S=N and I=1

Overall transmission rate:

$$\beta$$

So

$$R_0 = \frac{\beta}{\gamma}$$

Reproduction number

Deriving R0 from compartmental models

! If we change the model, we (usually) change the formula for R0!

Model SI

$$\frac{dS}{dt} = -\frac{\beta}{N} S_t I_t$$

$$\frac{dI}{dt} = \frac{\beta}{N} S_t I_t - \gamma I_t$$

With S=N and I=1

Overall transmission rate:

$$\beta$$

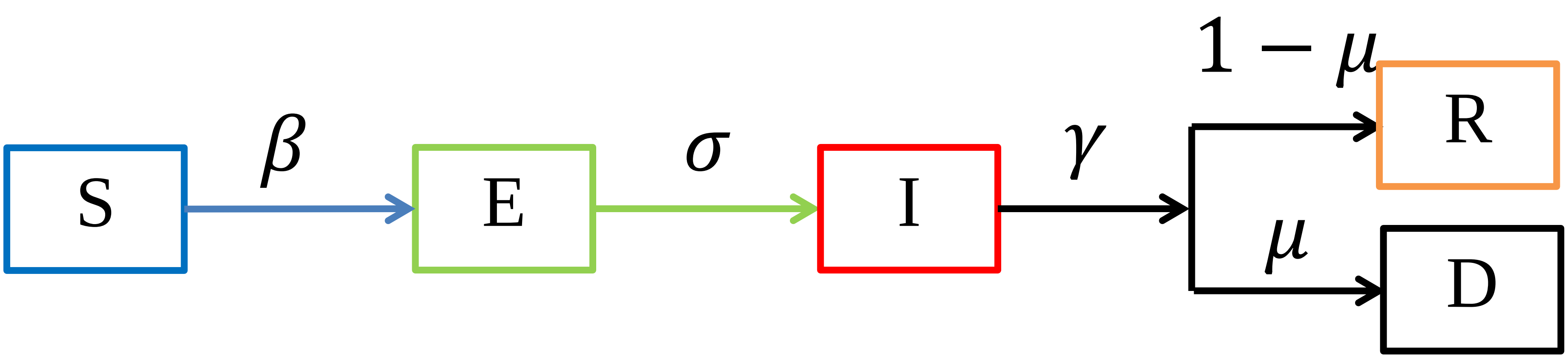
So

$$R_0 = \frac{\beta}{\gamma}$$

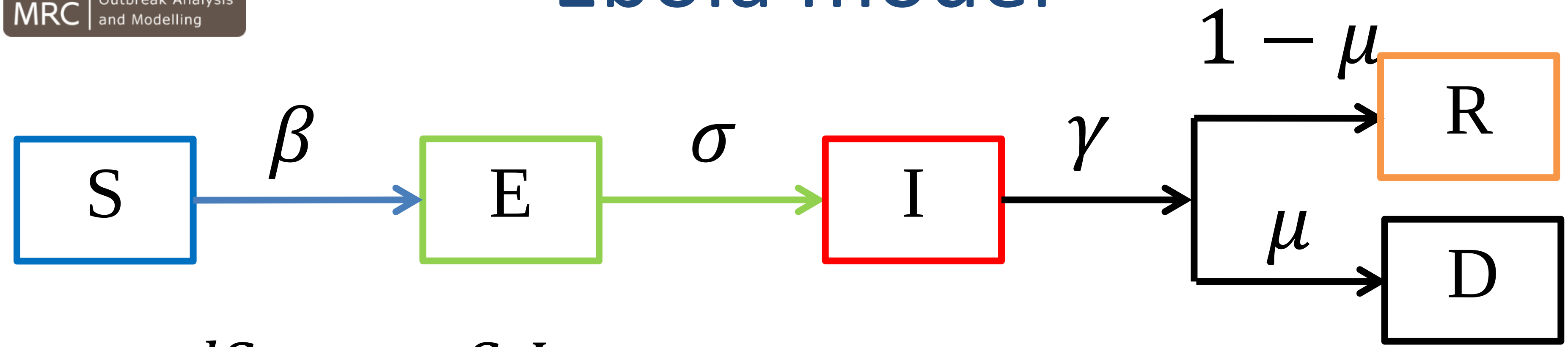
Ebola model

Natural history of the disease:

1. A susceptible person becomes infected (β)
2. Latency period ($1/\sigma$) – or virus incubation period
3. Infectious period ($1/\gamma$): symptomatic, associated with large mortality and high viral load
4. Case fatality ratio (μ): proportion of death



Ebola model



$$\frac{dS}{dt} = -\beta \frac{S_t I_t}{N_t}$$

$$\frac{dE}{dt} = +\beta \frac{S_t I_t}{N_t} - \sigma E_t$$

$$\frac{dI}{dt} = +\sigma E_t - \gamma\, I_t$$

$$\frac{dR}{dt} = +(1-\mu)\gamma I_t$$

Model for contacts: ‘frequency dependent’

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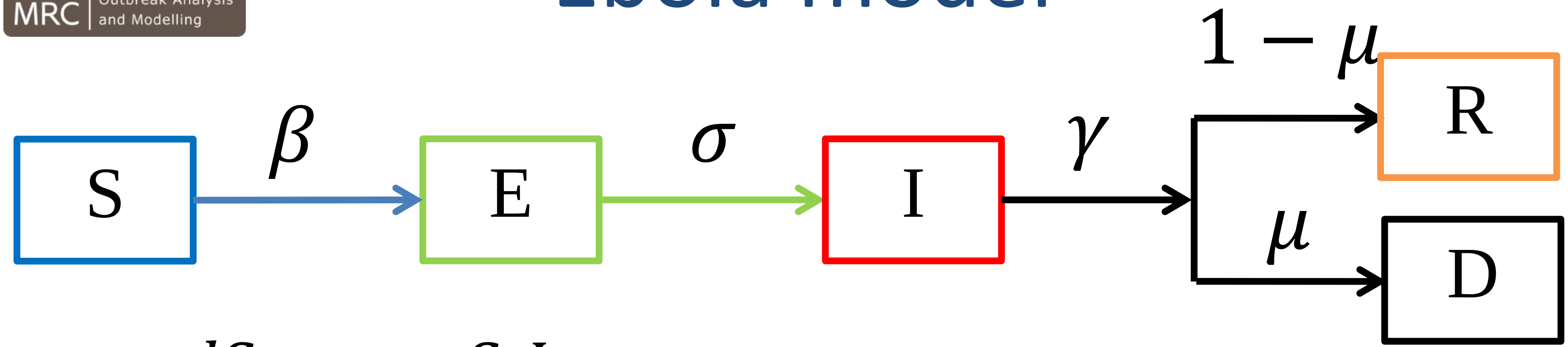
Ebola model



$$\frac{dS}{dt} = -\beta \frac{S_t I_t}{N_t}$$

$$\frac{dE}{dt} = +\beta \frac{S_t I_t}{N_t} - \sigma E_t$$

$$\frac{dI}{dt} = +\sigma E_t - \gamma\, I_t$$

$$\frac{dR}{dt} = +(1-\mu)\gamma I_t$$

Reproduction number:

$$R_0 = \beta \times {}^{1}\!/_{\gamma}$$

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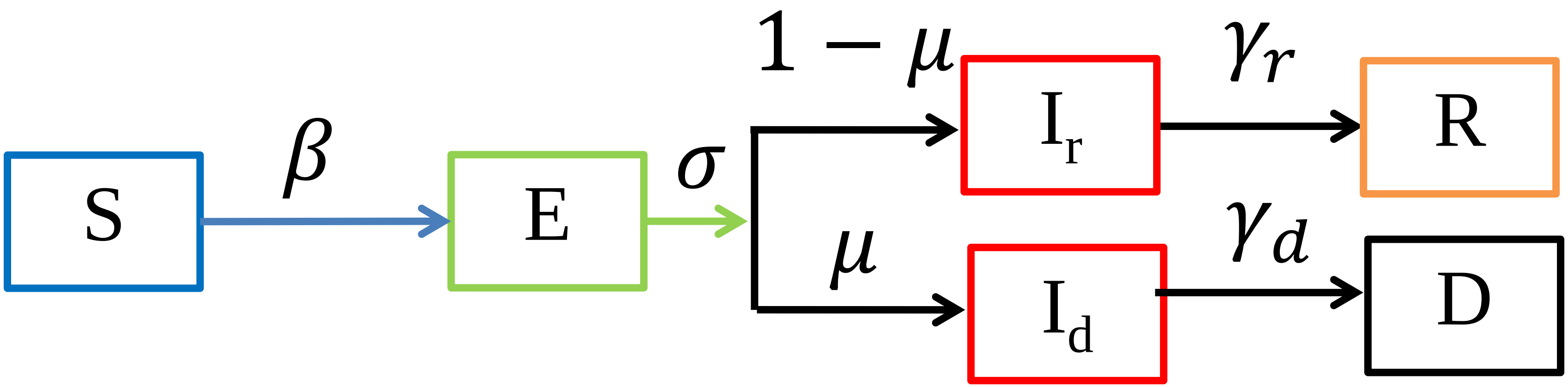
Ebola model

Increasing model complexity:

- delay onset/death ≠ delay onset/recovery



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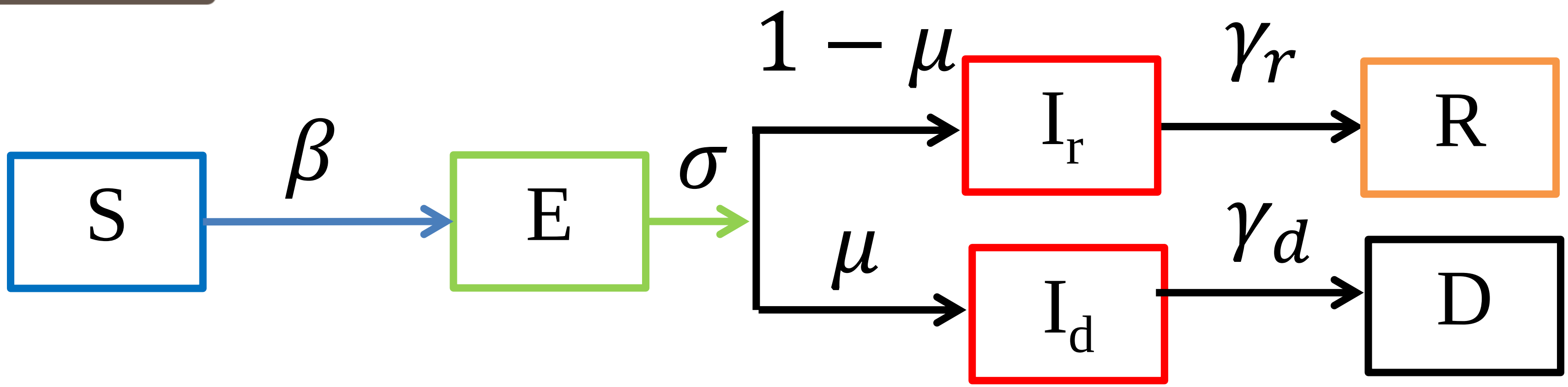
Ebola model



$$\frac{dS}{dt} = -\beta_d \frac{S_t I_{d,t}}{N_t} - \beta_r \frac{S_t I_{r,t}}{N_t}$$

$$\frac{dE}{dt} = +\frac{S_t}{N_t}\left[\beta_d I_{d,t} + \beta_r I_{r,t}\right] - \sigma E_t$$

$$\frac{dI_r}{dt} = +(1-\mu)\sigma E_t - \gamma_r I_{d,t}$$

$$\frac{dI_d}{dt} = +\mu\sigma E_t - \gamma_d I_{d,t}$$

$$\frac{dR}{dt} = +\gamma_r I_{d,t}$$

Reproduction number:

$$R_0 = (1-\mu)\frac{\beta_r}{\gamma_r} + \mu\frac{\beta_d}{\gamma_d}$$

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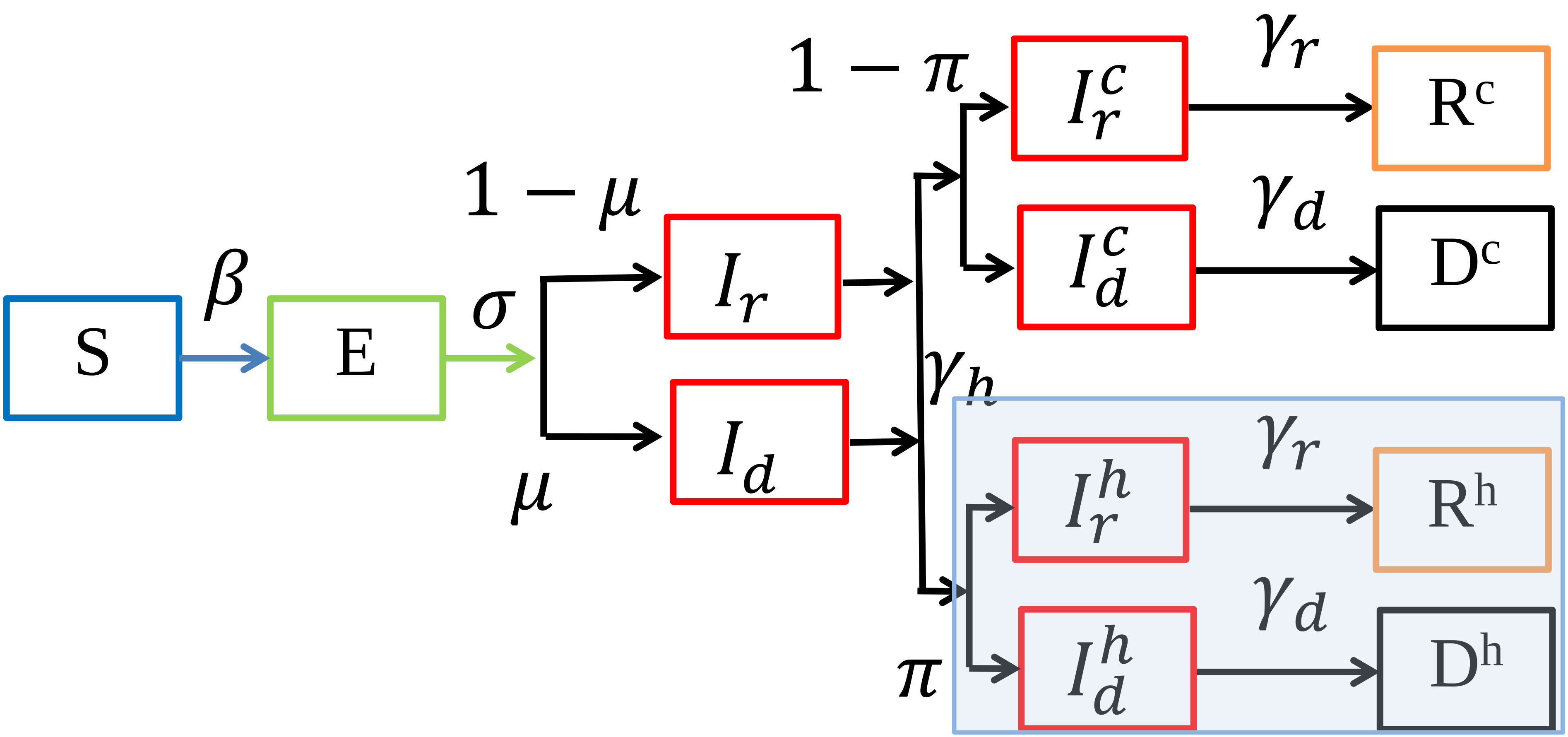
Ebola model

Increasing model complexity:

- delay onset/death ≠ delay onset/recovery
- once hospitalised/isolated, no further transmission



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Ebola model

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Pre-hospital

$$\frac{dS}{dt} = -\lambda_t \, S_t$$

$$\frac{dE}{dt} = \lambda_t \, S_t - \sigma E_t$$

$$\frac{dI_r}{dt} = (1-\mu)\sigma E_t - \gamma_h I_{r,t}$$

$$\frac{dI_d}{dt} = \mu\sigma E_t - \gamma_h I_{d,t}$$

with

$$\lambda_t = \beta_d \frac{\left(I_{d,t} + I_{d,t}^c\right)}{N_t} + \beta_r \frac{\left(I_{r,t} + I_{r,t}^c\right)}{N_t}$$

Stay in community

$$\frac{dI_r^c}{dt} = (1-\pi)\gamma_h I_{r,t} - \gamma_r I_{r,t}^c$$

$$\frac{dI_d^c}{dt} = (1-\pi)\gamma_h I_{d,t} - \gamma_d I_{d,t}^c$$

$$\frac{dR^c}{dt} = \gamma_r I_{r,t}^c$$

In hospital

$$\frac{dI_r^h}{dt} = \pi\gamma_h I_{r,t} - \gamma_r I_{r,t}^h$$

$$\frac{dI_d^h}{dt} = \pi\gamma_h I_{d,t} - \gamma_d I_{d,t}^h$$

$$\frac{dR^h}{dt} = \gamma_r I_{r,t}^h$$

Ebola model

Reproduction number:

- Someone who will die in community: $\beta_d \times \left[\frac{1}{\gamma_h} + \frac{1}{\gamma_d}\right]$
- Someone who will recover in community: $\beta_r \times \left[\frac{1}{\gamma_h} + \frac{1}{\gamma_r}\right]$

- Someone who will die in hospital: $\beta_d \times \left[\frac{1}{\gamma_h}\right]$
- Someone who will recover in hospital: $\beta_h \times \left[\frac{1}{\gamma_h}\right]$

Weighting to obtain reproduction number:

$$R_0 = \mu(1-\pi)\beta_d \left[\frac{1}{\gamma_h} + \frac{1}{\gamma_d}\right] + (1-\mu)(1-\pi)\beta_r \left[\frac{1}{\gamma_h} + \frac{1}{\gamma_r}\right] + \mu\pi\beta_d \left[\frac{1}{\gamma_h}\right] + (1-\mu)\pi\beta_r \left[\frac{1}{\gamma_h}\right]$$

$$= \mu\,\beta_d \left[\frac{1}{\gamma_h} + (1-\pi)\frac{1}{\gamma_d}\right] + (1-\mu)\beta_r \left[\frac{1}{\gamma_h} + (1-\pi)\frac{1}{\gamma_r}\right]$$

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Increase complexity

1. Impact of unsafe funeral - vaccination
2. Stochastic Model
3. Spatial Model
4. Individual based Model

Warning:

> ‘To explain a complex and poorly understood reality with a complex poorly understood model is not progress’
>
> John Maynard Smith

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Ebola model

practical